IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant(s):	Maria Adele Pacciarini et al.	**Examiner:**	Ganapathy Krishnan
Serial No.:	09/786,998	**Art Unit:**	1623
Filed:	June 14, 2001	**Docket:**	17815
For:	USE OF METHOXYMORPHOLINO DOXORUBICIN FOR THE TREATMENT OF A LIVER TUMOR	**Dated:**	August 14, 2007

Confirmation No.: 1122

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF UNDER 37 C.F.R. § 41.41(a)(1)

Sir:

This is a Reply Brief in response to the Examiner's Answer dated June 14, 2007, in the above-identified patent application. Pursuant to 35 U.S.C. §134 and 37 C.F.R. §41.41(a)(1), entry of this Reply Brief is respectfully requested.

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: August 14, 2007

Peter I. Bernstein

I. INTRODUCTION

This is in reply to the Examiner's Answer dated June 14, 2007 relative to the above-identified application. Since the Examiner's Answer does not contain a new ground of rejection, this Reply Brief is meant to supplement the arguments raised in the Appellants' Brief. Any argument not raised in the Reply Brief but presented in the Appellants' Brief is not to be considered withdrawn, but is incorporated by reference.

II. SUPPLEMENTAL ARGUMENTS

Upon review of the Examiner's Answer, Appellant wishes to address several points advanced by the Examiner in the Examiner's Answer.

1. Rejection of Claims 13 and 14 on appeal under 35 U.S.C. §103(a), over the combined teaching of Bargiotti et al., Kuhl et al., Nakamura et al. and Gorbunova et al.

The Examiner contends that a person skilled in the art would be motivated to make the compositions as instantly claimed since MMDX is structurally close to doxorubicin (DOX) and is known to be used in the treatment of tumors. Appellants emphasize that, in addition to the corresponding arguments raised in the Appellants' Brief, even if there is a structure and function similarity between MMDX and DOX, which is not the case[1], any such similarity is rebutted by the unexpected results obtained by utilization of the MMDX molecule over that of DOX. The Appellants respectfully observe that the optimum intravenous dose of MMDX is at least eighty

[1] Recall that MMDX contains a bulky methoxymorpholino group at position 3' of the sugar moiety whereas DOX contains an amino group. This fundamental structural difference between MMDX and DOX affects the functional interactivity with biological agents as discussed during the prosecution of the instant case.

times less than that of DOX, see Page 2, lines 7-9 of the instant specification. This dramatic difference in functionality of MMDX demonstrates far superior and unexpected efficacy over DOX, *in vivo*. This unexpected efficacy certainly would not have been appreciated by the skilled artisan at the time of the invention. As such, this remarkable efficacy rebuts any presumption of structural or functional obviousness.

Furthermore, Appellants respectfully submit that the Examiner's reasoning represents a hindsight appreciation of the instant invention. Where no suggestion indicates which of many possibilities is likely to be successful, it is inappropriate to conclude that a claimed invention would have been obvious simply because the inventor could have tried each of numerous possible choices until eventually arriving at a successful result. Any such picking and choosing among the prior art disclosures using the present application as a road map represents a hindsight analysis which is contrary to established case law. "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through a maze of prior art references, combining the right references in the right way so as to achieve the result of the claims at suit.'" Grain Processing Corp. v. American Maize-Prods. Co., 840 F.2d 902, 907, 5 USPQ2d. 1788, 1792 (Fed.Cir. 1988).

Appellants therefore submit that Claims 13 and 14 on appeal are non-obvious over the combined teaching of Bargiotti et al. taken with Kuhl et al., Nakamura et al., and Gorbunova et al.

2. Rejection of Claims 18, 20-23, 26 and 27 on appeal under 35 U.S.C.§103(a), over the combined teaching of Bargiotti et al., Kuhl et al., Nakamura et al. and Gorbunova et al.

The Examiner alleges that MMDX and DOX are not entirely distinguished compounds, based on purported similarity in structure and function. The Examiner further avers that a person skilled in the art would be motivated to use MMDX in an intrahepatic administration for the treatment of tumors since the prior art discloses administration and dosage details of DOX in the intrahepatic treatment of liver tumors. Appellants submit that the above remarks concerning the unexpected efficacy of MMDX rebut any presumption of structural or functional obviousness and apply equally well in this rejection, and therefore are incorporated therein.

Furthermore, Kuhl et al. teaches that MMDX is activated in the liver to a highly active metabolite. This teaching, together with the description of the present application, at Page 2, lines 10-19 and Page 7, lines 4-7, suggests that MMDX is transformed in the body into highly cytotoxic metabolites. Moreover, the Examiner admits that Gorbunova et al. teaches that intra-arterial infusion chemotherapy allows for the creation of extremely high concentrations of the antitumor agents in the organ affected by the tumor. Therefore, in view of the teachings from the prior art that extremely high concentrations of MMDX would be created around the liver by intrahepatic administration of MMDX, and MMDX would be transformed into highly cytotoxic metabolites, one skilled in the art would not have been motivated to even attempt to try to use MMDX in an intrahepatic administration for the treatment of liver tumors as claimed in the instant application, since such treatment would cause significant

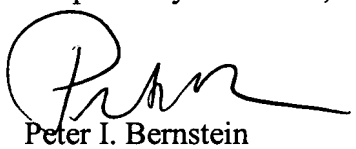
toxicity to the human body. Stated differently, the cited art provides a clear teaching away from the presently claimed invention.

Appellants therefore submit that Claims 18, 20-23, 26 and 27 on appeal are non-obvious over the combined teaching of Bargiotti et al. taken with Kuhl et al., Nakamura et al., and Gorbunova et al.

III. CONCLUSION

The above arguments establish that claims 13-14 and 18-31 on appeal are patentable over the combined teaching of Bargiotti et al., Kuhl et al., Nakamura et al. and Gorbunova et al. In view of the remarks set forth in this Reply Brief, Appellants respectfully request that the rejections under 35 U.S.C. § 103(a) citing the aforementioned references made in the Final Rejection dated May 1, 2006, and in the Advisory Action of December 20, 2006, be reversed by the Board of Patent Appeals and Interferences.

Respectfully submitted,



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